UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,756	06/29/2006	Derek Hart	18638	2472

23389 7590 10/16/2008

SCULLY SCOTT MURPHY & PRESSER, PC
400 GARDEN CITY PLAZA
SUITE 300
GARDEN CITY, NY 11530

EXAMINER	
JUEDES, AMY E	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
10/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,756	HART, DEREK	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12, 14, and 16-32* is/are rejected.

7)☒ Claim(s) *13 and 15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-32 are pending and are under examination.

2. Claims 13 and 15 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim.. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

3. Claim 24 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 24 depends from claim 27, and recites that the antibody is specific for CMRF-44 or its functional equivalent. However, claim 27 is already limited to a method employing an antibody specific for CMRF-44 or its functional equivalent. Additionally, it is noted that claim 24 does not depend from a preceding claim, but rather depends from claim 27. A series of singular dependent claims is permissible in which a dependent claim refers to a preceding claim which, in turn, refers to another preceding claim.

A claim which depends from a dependent claim should not be separated by any claim which does not also depend from said dependent claim. It should be kept in mind that a dependent claim may refer to any preceding independent claim. In general, applicant's sequence will not be changed. See MPEP § 608.01(n).

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 31-32 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 31-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 31-32 provide for the use of an antibody to CMRF-44, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

7. Claims 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 25 recites the limitation "said subject" in line 2. There is insufficient antecedent basis for this limitation in the claim.

8. Claims 16 and 27-30 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The claims are incomplete for omitting essential steps. While all of the technical details need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced.

A) Claim 16 is drawn to a method of modulating the immuno-activity of an APC and/or lymphocyte. However, the only recited method step is contacting the APC with a monoclonal antibody to induce lysis of the APC. This might encompass contacting an isolated APC in vitro with said antibody. It is unclear how this could result in the modulation of a lymphocyte in the absence of an additional method step (for example, administration of the antibody in vivo, or a method step involving contacting the antibody treated APCs with the lymphocytes).

B) Claims 27-30 are drawn to a method for the therapeutic treatment of a condition characterized by the aberrant, unwanted, or otherwise inappropriate immuno-activity of graft. However, the only recited method step involves contacting the graft with an antibody specific for CMRF-44. This might encompass contacting a graft in vitro with an antibody, and in the absence of additional method steps it is not clear how the method could result in the therapeutic treatment of a condition. For example, the claims do not recite that the graft is

contacted in a subject (i.e. by administering the antibody to a subject).

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-12, 14, and 16-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, there is insufficient written description to demonstrate that applicant was in possession of the claimed genus of “agents” or “immunointeractive molecules” which bind to “cell-surface activation molecules” or “APC surface activation molecules”, “functional equivalents” of an antibody, monoclonal antibodies to a “cell surface antigen”, or antibodies specific for CMRF44 or its “functional equivalent” on an APC.

The guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus

Claims 1-6, 11-12, and 20-22 are drawn to methods employing an "agent" or "immunointeractive molecule" that binds to a cell-surface molecule. This might encompass a broad genus of structurally different compounds, such as antibodies, peptides, protein ligands, and small molecules. The specification does not disclose a correlation between the structure of the “agents" or “immunointeractive molecules” and the function of binding to a

cell-surface molecule. Furthermore, the specification only discloses a single species of “agent” or “immunointeractive molecule”, i.e. antibodies. The disclosure of a single species is not sufficiently representative of the broad range of structurally different “agents” or “immunointeractive molecules” encompassed by the claims.

Additionally, claims 1-8, 11-12, 16, and 18-23 are drawn to methods comprising contacting an APC with an agent, immunointeractive molecule, or antibody that binds to a "cell-surface activation molecule”, a “cell surface antigen”, or an “APC surface activation molecule”. Claims 1-8, 11-12, 16, and 18-19 do not even specify that the activation molecule or surface antigen actually be expressed by the APC. The specification on page 14 defines “cell-surface activation molecules” as a molecule the expression of which is upregulated upon stimulation of an APC. However, the definition provided in the specification does not explicitly set forth that the activation molecules are expressed by the APCs. For example, the activation molecules might encompass molecules expressed by T cells, which are upregulated in response to stimulation with APCs. Thus, it appears claims 1-8, 11-12, 16, and 18-19 encompass contacting APCs with an agent, immunointeractive molecule, or antibody that binds to any cell-surface activation molecule or cell surface antigen, not only those expressed by APCS. This might encompass a broad range of agents/antibodies that bind to structurally and functionally different molecules expressed by a broad range of cell types. Furthermore, even though claims 20-23 are limited to agents/antibodies that bind to "APC surface activation molecules", the claims still encompass antibodies/agents specific for a broad range of structurally and functionally different APC surface activation molecules. Furthermore, claim 1-8, 11-12, and 20-23 encompass methods employing an agent/antibody that binds to activation molecule and prevents, inhibits or down-regulates the functional activities of an antigen presenting cell. The specification does not disclose a correlation between the structure of said agents/antibodies and said function, nor is there an art recognized correlation between structure and function. Likewise, claim 16 recites that the antibodies induce cell lysis. While antibodies (for example, those linked to a toxin) are known in the art to be capable of inducing lysis upon binding to a cell, claim 16 encompasses inducing lysis of an APC using an antibody that binds to any cell surface antigen. For example, the claim might encompass contacting an APC with an

antibody that activates lymphocytes in order to induce cell death of the APC by the activated lymphocytes. The specification does not disclose a correlation between the structure of said antibodies to any cell surface antigen, and the function of inducing cell death of APCs. Additionally, the specification only discloses a single species of cell surface activation molecule, CMRF-44, a marker of dendritic cells. This is not sufficiently representative of agents/antibodies that bind to the broad genus of structurally different cell surface antigens, surface activation molecules, or APC surface activation molecules encompassed by the instant claims

Furthermore, claims 7-10 and 14 are drawn to methods employing a antibody specific for a cell-surface activation molecule or an antibody specific for CMRF-44 "or functional equivalent thereof". The specification on page 15 discloses that functional equivalents should be understood as molecules exhibiting any one or more of the functional activities of the molecule, that may be derived from any source. Thus, the claims encompass any molecule capable of binding to a cell-surface activation molecule, or to CMRF-44. The claims might encompass structurally different molecules including protein ligands, peptides, or even small molecules. The specification does not provide any correlation between the structure of the members of the claimed genus and the function of binding to cell surface activation molecules or to CMRF-44. Furthermore, there is no art recognized correlation between said structure and function. Additionally, the only "functional equivalents" disclosed by the specification are antigen binding antibody fragments. This is not representative of the structurally different "functional equivalents" encompassed by the claims.

Additionally, claims 17-19 and 24-30 are drawn to methods employing an antibody specific for a "functional equivalent" of CMRF-44. This might encompass antibodies to structurally different cell surface receptors on antigen presenting cells. The specification does not disclose a correlation between the structure of CMRF-44 and its function, and thus there is no disclosed correlation between antibodies that bind to CMRF-44 or its "functional equivalent". Additionally, the specification does not disclose a single species of antibody specific for the "functional equivalent" of CMRF-44. Thus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was

in possession of the claimed genus. See Eli Lilly, 119 F. 3d 1559, 43, USPQ2d 1398.

11. Claims 1-12, 14, 16-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method of downregulating the immuno-activity of an APC comprising contacting said APC with an antibody or fragment thereof that binds to an APC cell surface activation molecule or APC cell surface antigen, wherein the antibody is capable of inducing lysis of the APC, a method of downregulating the immuno-activity of an APC comprising contacting said APC with an antibody or fragment thereof that is specific for CMRF-44 and in turn inhibits or down-regulates one or more functional activities of said cell, a method for downregulating an immune response in a subject comprising administering to the subject an antibody or fragment thereof which binds with an APC surface activation molecule (including CMRF-44), wherein said antibody/fragment induces cell lysis, a method for down-regulating the immuno-activity of a graft and a method of the treatment of a condition characterized by the aberrant, unwanted, or otherwise inappropriate immunoactivity of an immuno-competent graft in a subject comprising administering to the subject an antibody specific for CMRF-44, or an antibody specific for an APC surface activation molecule, wherein the antibody induces APC lysis,

does not reasonably provide enablement for a method for modulating the immuno-activity of an APC comprising contacting said cell with an agent with binds to a cell surface activation molecule and prevents, inhibits, or down-regulates one or more functional activities of said cell, a method of modulating the immuno-activity of an APC and/or lymphocytes comprising contacting said APC with an antibody to a cell surface antigen for a time and under conditions sufficient to induce lysis of said cell, a method for modulating an immune response in a subject comprising administering an agent which binds to an APC surface activation molecule and prevents, inhibits, or otherwise down-regulates one or more functional activities of an APC, and methods employing an antibody specific for a functional equivalent of CMRF-44.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the

claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, in re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

The specification provides insufficient guidance to enable claims drawn to the method as broadly claimed. Claims 1-12, 14, and 16-23 are drawn to a method of "modulating" the immuno-activity of APC or an immune response in a subject with an agent that prevents, inhibits, or downregulates the functional activities of the cell, or a method of "modulating" the immuno-activity of an APC and/or lymphocyte with an antibody that induces cell lysis. The term "modulates" encompasses both an increase and a decrease in the immuno-activity of the cell or the immune response. While downregulating the function of APCs, or causing lysis of APCs might be expected to result in a decrease in immune activity of said cells, or to result in a decreased or suppressed immune response, it is not clear how the immuno-activity or immune response could be increased, as is encompassed by the instant claims.

Additionally, claims 1-8, 11-12, 16, and 18-19 are drawn to a method of modulating the immuno-activity of an APC comprising contacting an APC with an agent or antibody that bind to a cell-surface activation molecule or a cell surface antigen. The specification on page 14 defines "cell-surface activation

molecules" as a molecule the expression of which is upregulated upon stimulation of an APC. However, this definition does not limit said surface activation molecules (or cell surface antigens) to those expressed by the APCs themselves. For example, the claims might encompass contacting a population of cells, including an APC with an antibody that activates another cell type to induce APC lysis or down-regulate APC function. While it would be reasonable to downregulate the immunoactivity of an APC using an antibody specific for an APC cell surface antigen, wherein the antibody induces lysis of the APC, the instant claims in their breadth encompass using an antibody or agent specific for any cell surface molecule (even those expressed by other cells). Furthermore, claims 1 and 20 encompass modulating APC activity by methods other than inducing cell lysis (for example, by contacting an APC with an agent that downregulates the functional activities of an APC, or even agents that "prevent" an activity). Antigen presenting cells are extremely complex, existing as a myriad of different subsets with different phenotypes, and have diverse functional properties ranging from stimulating an immune response to inducing tolerance (see Novak et al., 2008 and Sumpter et al., 2007). Thus, the ability to modulate the immuno-activity of an APC using an agent or antibody specific for any cell surface molecule by mechanisms including downregulating or inhibiting the function of said APC is extremely unpredictable. Additionally, the claims encompass not only downregulating the activities of a cell, but preventing said activities. This encompasses completely preventing any functional activity of the cells using an antibody. While it may be possible to downregulate or inhibit the activities of said cells by inducing cell lysis with an antibody (for example, an antibody conjugated to a toxin), a complete prevention would require lysing every cell. Furthermore, claim 16 encompass modulating the immuno-activity of a lymphocyte, but the only recited method step involves contacting an APC with an antibody. It is not clear how the method could result in the modulation of a lymphocyte, such as a T cell, as is encompassed by the claims. Furthermore, the instant specification only discloses a single example of using an antibody specific for CMRF-44 to induce lysis of APCS, hence downregulating (but not "preventing") the immunoactivity of said APC. The specification further demonstrates that APC populations treated with said antibody have a reduced ability to stimulate T lymphocytes. However, this is not commensurate in scope with the instant claims which encompass modulating (both increasing and decreasing) the immuno-activity of an APC or a

lymphocyte employing any agent that binds to any cell surface activation molecule or surface antigen to prevent or inhibit any functional activity of the cell.

Additionally, the claims 1-12, 14, and 20-23 are drawn to a method of modulating the immuno-activity of an APC or a method for modulating the immune response employing an "agent" or "immunointeractive" molecule that binds to a cell surface activation molecule, or a "functional equivalent" of an antibody, including an antibody specific for CMRF-44. The specification on page 13 states that an “agent” refers to any proteinaceous or non-proteinaceuous molecule which binds to a cell surface activation molecule. The specification on page 15 discloses that functional equivalents should be understood as molecules exhibiting any one or more of the functional activities of the molecule (i.e. antibodies) that may be derived from any source. Thus, the agents, immunointeractive molecules, and functional equivalents, encompass any molecule that binds to a cell surface activation molecule or to CMRF-44. For example, the claims might encompass methods employing the natural ligand of cell surface activation molecules, such as CMRF-44, as the “agent” or "functional equivalent". Likewise, the claims might encompass methods employing small molecules that bind to cell surface activation molecules, including CMRF-44. However, the state of the art is such that the CMRF-44 is an antigen of unknown function (see Vockovic et al., 2001, page 2954). Additionally, there are no known small molecule "agents" that bind to CMRF-44. Additionally, the instant specification does not provide any guidance as to how to identify “agents” or "immunointeractive molecules" that bind to a cell surface activation molecule, or "functional equivalents" of an antibody. Additionally, the only “agents” and “immunointeractive molecules” disclosed by the instant specification are antibodies, and the only "functional equivalents" disclosed by the instant specification are antigen binding antibody fragments. Given the level of unpredictability in the art (i.e. the unknown structure of other cell surface binding “agents” including those that bind to CMRF-44), it would require undue experimentation to make other “agents”, “immunointeractive molecules” or “functional equivalents”, as is encompassed by the instant claims.

Furthermore, claims 17-19 and 24-30 are drawn to methods employing an antibody specific for a “functional equivalent” of CMRF-44. The specification on page 15 discloses that functional

equivalents should be understood as molecules exhibiting any one or more of the functional activities of the molecule. Thus, the claims are drawn to methods employing antibodies specific for molecules that exhibit one or more functional activities of CMRF-44. However, the instant specification only discloses that CMRF-44 is a dendritic cell marker. The specification does not disclose any functional attributes of CMRF-44 (other than its expression pattern), and the state of the art is such that CMRF-44 is an antigen of unknown function (see Vockovic et al., 2001, page 2954). Thus, while it might be possible to identify antigens that exhibit an equivalent expression pattern as CMRF-44, it would require undue experimentation to identify molecules that are "functional" equivalents of CMRF-44, as broadly claimed. Thus, based on the unpredictability of the art and the lack of guidance by the instant specification, it would require undue experimentation to practice the invention as broadly claimed.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-12 and 16-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Koppi et al., 2001, Immunol. and Cell Biol.

Koppi et al. teach a method of inducing dendritic cell lysis (i.e. downregulating the immuno-activity of an antigen presenting cell) comprising contacting human dendritic cells with a monoclonal antibody specific for CMRF-44. Koppi et al. teach that the lysed dendritic cells are CD11c positive (i.e. myeloid DCs).

Thus, the reference clearly anticipates the invention.

14. Claims 1-8, 11-12, and 16-30 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/24078.

WO 99/24078 teaches a method of depleting antigen presenting cells (i.e. a method of downregulating the immuno-activity of an antigen presenting cell) comprising contacting

the antigen presenting cell with an antibody specific for an antigen expressed by APCs (see page 3 and 20-21 in particular). WO 99/24078 teaches that the depleted antigen presenting cells can be dendritic cells, B cells, or macrophages (see page 3 in particular). WO 99/24078 teaches that the antigen presenting cells may be depleted using an antibody immunotoxin that binds to various antigen presenting cell markers such as MHC, CD11c, and B7 (i.e. surface activation molecules or surface antigens, see page 10-11 in particular). Thus, the method of WO 99/24078 results in the depletion of CD11c expressing myeloid dendritic cells, as recited in the instant claims. Additionally, WO 99/24078 teaches depleting human cells, and that the method results in the killing of the APC (i.e. cell lysis, see page 3 and 10, in particular). WO 99/24078 also teaches monoclonal antibodies (see page 12 in particular). WO 99/24078 also teaches depleting the APCs in vivo (i.e. modulating an immune response in a subject) to treat graft versus host disease resulting from an alloimmune attack on host tissues initiated by host-APCs. (see page 9, 20 and 22 in particular). WO 99/24048 teaches treating said graft versus host disease (i.e. a method of down regulating the immunoactivity of a graft or treating a condition characterized by the inappropriate immunoactivity of a graft) by administering the antibodies to a subject (see page 20 and 22 in particular). WO 99/24078 also teaches that the antibodies can be administered concurrent with allogenic bone marrow transplantation (i.e. the administration of the antibodies results in the "contact" of the bone marrow graft with the antibodies, see page 20 in particular). Additionally, claims 17 and 24-30 are included since WO 99/24078 teaches antibodies specific for CD11c, which can be considered a "functional equivalent" of CMRF-44 on an APC, since both CMRF-44 and CD11c display a similar expression pattern (i.e. they are dendritic cell specific markers).

Thus, the reference clearly anticipates the invention.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12, 14, and 16-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/24078, in view of U.S. Patent 5,876,917, as evidenced by Flavell et al., 1998, Cancer Research.

The teachings of WO 99/24078 are described above.

WO 99/24078 does not teach an antibody specific for CMRF-44.

The '255 patent teaches an antibody specific for CMRF-44 which is expressed by activated antigen presenting cells, including dendritic cells (see column 3 in particular). The '255 patent further teaches that CMRF-44 is a marker that can be used to specifically identify allostimulatory populations of antigen presenting cells.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to perform the therapeutic method of treating graft versus host disease by administering an antibody specific for an antigen presenting dendritic cell, as taught by WO 99/24078, using the CMRF-44 antibody taught by the '255 patent. The ordinary artisan would have been motivated to do so, and have a reasonable expectation of success, since WO 99/24078 teaches that antibody depletion of antigen presenting cells that initiate an alloimmune attack is useful for treating graft versus host disease, and the '255 patent teaches that antibodies specific for CMRF-44 identify activated, allostimulatory populations of antigen presenting cells. Additionally, it would have been obvious to use the CMRF-44 antibody of the '255 patent conjugated to an immunotoxin as a means to deplete APCs, as taught by WO 99/24078. As evidenced by Flavell et al., administration of immunotoxin antibodies results in lysis of target cells by a variety of mechanisms, including antibody-dependent cellular cytotoxicity.

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not

patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1-12, 14, and 16-30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 8-13, 15, and 20 of copending Application No. 10/524,716, in view of U.S. Patent 5,876,917. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 9 of the ‘716 application is drawn to a method of modulating the immune response comprising administering an antibody which binds to a dendritic cell surface activation molecule. It would have been obvious to use the CMRF-44 antibody of the '917 patent in said method, since the '917 patent teaches that CMRF-44 is an activation molecule expressed by dendritic cells. Said method would result in the "contact" of dendritic cells with the antibody in vivo. Additionally, the '716 application claims a method of modulating the immuno-activity of a dendritic cell, a method of down-regulating the immuno-activity of a graft, and a method of treating a condition characterized by the inappropriate immunoactivity of a graft comprising contacting the cell/graft with an antibody which binds to CD83 (i.e. a cell surface "activation molecule") or comprising administering said CD83 antibody. The '716 patent further claims that the antibody causes antibody-dependent cell mediate cytotoxicity, and that the cell can be a human cell. Additionally, since CD83 is expressed by dendritic cells, it can be considered a “functional equivalent” of CMRF-44, as recited in the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy Juedes, whose telephone number is 571-272-4471. The examiner can normally be reached on 6am - 2pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Amy E. Juedes
Patent Examiner
Technology Center 1600
/Amy E. Juedes/
Examiner, Art Unit 1644